Insertion was, however, observed with bidentate phosphane ligands.

For the alternating copolymerization of imine with carbon monoxide to proceed, the subsequent insertion of carbon monoxide into the palladium(II)–carbon bond of the imine-inserted product must occur. In preliminary experiments, we did not observe carbon monoxide insertion in species **3a** at ambient temperature. We ascribe our failure to the strong binding of the carbonyl group of the amide fragment to the metal, thereby preventing the coordination of an incoming carbon monoxide molecule. While a similar coordination of the carbonyl group also occurs in the intermediates involved in the alternating copolymerization of alkenes and carbon monoxide,[5a, 6, 7] the difference lies in the greater negative charge and, therefore, stronger coordinating ability of the carbonyl oxygen of an amide fragment. Interestingly, the insertion of carbon monoxide apparently occurs readily in analogous species where the amide carbonyl is not coordinated to the metal.[8]

Experimental Section

Synthesis of **1a–k**: A solution of $AgBF_4$ in acetonitrile was added to a solution of $L_2Pd(Me)(Cl)$ (1 equiv) and imine (1 equiv) in dichloromethane. After this had been stirred for 15 min, the AgCl was removed by filtration. The resulting complex was isolated by removing the solvent and drying under reduced pressure for 1 d.

Reaction of **1a–k** with carbon monoxide: The complex **1a–k** (0.10 g) was dissolved in $CDCl_3$ and placed in a 22 mL Parr bomb, which was then charged with 3.4 bar of carbon monoxide. The mixture was allowed to stand at ambient temperature for 1 d. The excess carbon monoxide was then released, the solution filtered to remove any metallic palladium, and the product characterized by ^1H, $^{31}P\{^1H\}$, and $^{13}C\{^1H\}$ NMR spectroscopy. Reactions were also run with ^{13}C-labeled carbon monoxide.

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Maracin and Maracen: New Types of Ethynyl Vinyl Ether and α-Chloro Divinyl Ether Antibiotics from *Sorangium cellulosum* with Specific Activity Against Mycobacteria**

Martina Herrmann, Bettina Böhlendorf, Herbert Irschik, Hans Reichenbach, and Gerhard Höfle*

Dedicated to Professor Meinhart H. Zenk on the occasion of his 65th birthday

Even in highly developed industrial countries, tuberculosis is still one of the most common causes of death due to infection.[1] The causative pathogen, *Mycobacterium tuberculosis*, can only be completely eliminated by a lengthy course of treatment despite the use of highly active antibiotic combination preparations (rifampicin, streptomycin, isoniazide etc.), since its growth is particularly slow and it is protected by a wax-containing cell wall.[2] The same is true for leprosy which is also caused by mycobacteria.[3] In AIDS, increasing occurrence of multiresistant *M. tuberculosis* strains and atypical mycobacterial infections is a particular danger.[2, 4] New types of antibiotics are urgently needed to treat such infections, in order to aid patients in individual cases and in the long term, to prevent the spread of resistant pathogen strains.

During a screening program using the nonpathogenic *Mycobacterium phlei* as indicator organism, we discovered

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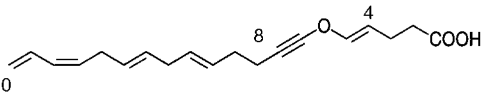
in the *Sorangium cellulosum* strains So ce880 and So ce1128 a new group of antibiotics with specific activity against mycobacteria. TLC and HPLC analysis revealed compounds in the culture extracts of both strains that, according to polarity and UV spectra, are very similar to one another and to which the biological activity could be assigned.

To isolate the compounds, ethyl acetate extracts of 100 L cultures of the production strains So ce880 and So ce1128 were fractionated on Sephadex LH-20 (methanol) and RP-18 silica gel (methanol/0.05 M ammonium acetate buffer (80/20)). The main active components maracin A (**1**, 116 mg, So ce880) and maracen A (**2**, 731 mg, So ce1128) thereby were obtained as colorless oils.[5, 6] According to their migration behavior on silica gel and RP-18 silica gel, **1** and **2** are lipophilic carboxylic acids.



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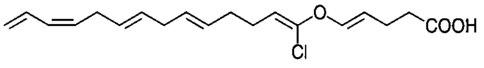

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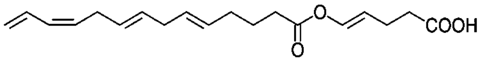

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Table 1. Selected physical and spectroscopic data for maracin A (**1**) and maracen A (**2**).

1: $C_{19}H_{24}O_3$ ($M_r = 300.40$); colorless oil; TLC: $R_f = 0.53$ (silica gel, dichloromethane/acetone/methanol (85/15/5));[a] IR (KBr): $\tilde{\nu} = 2280$, 1712, 1673, 1662, 1222 cm^{-1}; UV/Vis (methanol): λ_{max} ($\log\varepsilon$) = 208 (4.41), 227 nm (4.47); ^{1}H NMR (300 MHz, CDCl$_3$): $\delta = 2.43$ (t, $J = 7.3$ Hz, 2H, 2-H), 2.31 (q, $J = 7.3$ Hz, 2H, 3-H), 5.57 (dt, $J = 12.0$, 7.3 Hz, 1H, 4-H), 6.27 (d, $J = 12.0$ Hz, 1H, 5-H), 2.22 (m, 4H, 9-H, 10-H), 5.43 (m, 5H, 11-, 12-, 14-, 15-, 17-H), 2.75 (m, 2H, 13-H), 2.88 (m, 2H, 16-H), 6.02 (t, $J = 11.0$ Hz, 1H, 18-H), 6.62 (dt, $J = 16.8$, 11.0 Hz, 1H, 19-H), 5.19 (d, $J = 16.8$ Hz, 1H, 20-H$_a$), 5.10 (d, $J = 11.0$ Hz, 1H, 20-H$_b$); ^{13}C NMR (75.5 MHz, CDCl$_3$): $\delta =$ 178.0 (C-1), 34.1 (C-2), 21.8 (C-3), 108.7 (C-4), 144.6 (C-5), 84.1 (C-7), 44.1 (C-8), 17.6 (C-9), 27.2 (C-10), 128.8 (C-11), 128.8 (C-12), 30.5 (C-13), 129.2 (C-14), 128.3 (C-15), 30.8 (C-16), 130.3 (C-17), 129.6 (C-18), 132.1 (C-19), 117.4 (C-20); DCI-MS (NH$_3$): $m/z = 299.1644$ (calcd. for $[M-H]^-$: 299.1647)

2 (only data differing from **1** are given): $C_{19}H_{25}O_3Cl$ ($M_r = 336.86$); colorless oil; TLC: $R_f = 0.55$ (silica gel, dichloromethane/acetone/methanol (85/15/5));[a] IR (KBr): $\tilde{\nu} = 1711$, 1654, 1154 cm^{-1}; UV/Vis (methanol): λ_{max} ($\log\varepsilon$) = 205 (4.25), 224 nm (4.22); ^{1}H NMR (300 MHz, CDCl$_3$): $\delta = 2.29$ (q, $J = 7.2$ Hz, 2H, 3-H), 5.22 (dt, $J = 12.1$, 7.2 Hz, 1H, 4-H), 6.26 (d, $J = 12.1$ Hz, 1H, 5-H), 5.14 (overlapping, 1H, 8-H), 2.14 (m, 4H, 9-H, 10-H), 5.41 (m, 5H, 11-, 12-, 14-, 15-, 17-H), 2.74 (m, 2H, 13-H); ^{13}C NMR (75.5 MHz, CDCl$_3$): $\delta = 178.5$ (C-1), 34.3 (C-2), 22.5 (C-3), 110.3 (C-4), 143.2 (C-5), 141.5 (C-7), 109.7 (C-8), 27.3 (C-9), 26.4 (C-10), 129.0 (C-11), 128.6 (C-12), 30.4 (C-13); DCI-MS (NH$_3$): $m/z = 336.1449$, 338 (calcd for $[M(^{35}Cl)]^-$: 336.1492)

[a] Detection with vanillin/sulfuric acid, violet-red color on heating to 120 °C.

In the mass spectrum (direct chemical ionization, DCI) of maracin **1**, a molecular ion is observed ($m/z = 299.1644$ for $[M-H]^-$) that corresponds to the empirical formula $C_{19}H_{24}O_3$, from which eight double bond equivalents can be derived. The 2D NMR spectra indicate a terminal conjugated diene unit, two double bonds isolated by methylene groups, and a carboxy group as structural elements. The three remaining double bond equivalents can be assigned to an asymmetric substituted vinyl group and an ethynyl group, the latter documented by a conspicuous absorption band at 2280 cm^{-1} in the IR spectrum. Together, both form an ethynyl-*trans*-vinyl ether, which is a very unusual structural element for a natural substance. This assignment is supported by the chemical shifts of the C-4 and C-5 atoms (108.7 and 144.6 ppm) and the 4-H and 5-H atoms (5.57 and 6.27 ppm), the vicinal coupling constant $J_{4\text{-H},5\text{-H}} = 12.0$ Hz,[7] and chemical shifts of the C-7 and C-8 atoms (84.1 and 44.1 ppm, Table 1). In agreement with this, ^{13}C-labeled **1** (see below) shows a C-7,C-8 coupling of 225 Hz.[8a]

In contrast to **1**, a molecular ion of $m/z = 337/339$ for $[M-H]^-$ occurs in the DCI mass spectrum of maracen **2**. The relative molecular mass, the isotope pattern of the molecular ion, and the absence of an acetylene band in the IR spectrum of **2** point to a chloro divinyl ether with the empirical formula $C_{19}H_{25}O_3Cl$. Its structure differs from maracin **1** in the NMR spectrum only in the replacement of the alkynyl by a α-chlorovinyl group, which shows chemical shifts of 141.5 and 109.7 ppm for the C-7 and C-8 atoms and 5.14 ppm for the H-8 atom. Determination of the configuration at the trisubstituted C-7,C-8 double bond was not possible from the NMR data. Thus attempts were made to synthesize both the (7*E*) and the (7*Z*) isomers of **2** by HCl addition at the triple bond of **1**. This was achieved by reaction of maracin **1** with lithium chloride in acetic acid; a mixture of the two isomers was obtained in a ratio of (7*E*):(7*Z*) = 1.7:1.0.[9] Only by comparison of the NMR data of both isomers with the ^{1}H shifts calculated according to an incremental system[8b] was it possible to assign the (7*Z*) configuration to the natural product maracen **2** that we had isolated. Furthermore, the result of the HCl addition at **1** demonstrated that **2** is a genuine natural compound and not an artefact. Maracin **1** was recovered from either of the stereoisomers of **2** on reversal of the HCl addition by treatment with lithium diisopropylamide.[10] Acid-catalyzed reaction of **1** and **2** with water enabled isolation of the vinyl ester **3**, as expected, in addition to various cleavage products.[11] However, the hydrolysis of **1** proceded much slower than that of ethoxyacetylene, a reagent used in peptide synthesis for activation of carboxylic acids.[12]

Until now, there have been no examples for the biosynthesis of ether groups such as in **1** and **2**. Preliminary experiments with ^{13}C-labeled acetate indicate the same assembly pattern for **1** and **2** from nine intact acetate units and a carboxy group derived from the C-2 atom of a further acetate unit (Figure 1). The ether oxygen atom may be inserted in the C-5,C-6 bond of an intermediate C_{19} fatty acid by a mechanism related to the biosynthesis of divinyl ethers,[13] by fragmentation and Hock rearrangement[14] of a bisallylic 6-hydroperoxide. It is noteworthy that the only natural ethynyl ether known at present, the sesquiterpene lactiflorasin from

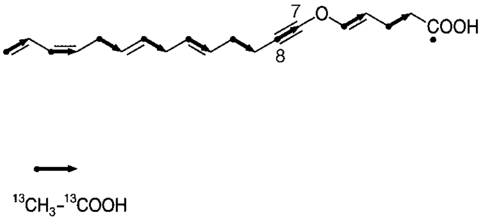

Figure 1. Biogenesis of maracin **1** from [1,2-$^{13}C_2$]acetate. The ^{13}C-labeled C_2 unit is represented by an arrow (blunt end: methyl C-atom, point: carboxy C-atom).

Artemisia lactiflora,[15] is, like **1**, also an ethynyl *trans*-vinyl ether. α-Chloro divinyl ethers were previously unknown as natural products.

According to initial results, maracin and maracen are active in vitro against the pathogen responsible for tuberculosis ($IC_{99} < 12.5\ \mu g\,mL^{-1}$);[16] whether they are also active in vivo has still to be demonstrated. With an in vitro toxicity of $\geq 24\ \mu g\,mL^{-1}$ against the mouse fibroblast line L929, they are supposedly of low toxicity for higher organisms and thus are possibly suitable for medical application.

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[6] In addition to the main components, the following side products were isolated: So ce880: maracin B (95 mg, 19,20-dihydro derivative of **1**), maracin C (15 mg, (17*Z*) isomer of **1**), maracin D (20 mg, (17*Z*) isomer of maracin B), maracin E (3 mg, (4*Z*) isomer of maracin B); So ce1128: maracen B (186 mg, 19,20-dihydro derivative of **2**), maracen C (66 mg, (17*Z*) isomer of **2**), maracen D (62 mg, (17*Z*) isomer of maracen B).
[7] The coupling constant $J_{4\text{-H},5\text{-H}}$ is 5.7 Hz for the *cis*-vinyl ether (maracin E)[6].
[8] a) Compare with the value of 216.5 Hz in ethoxyacetylene: see ref. [8c], p. 151; b) (7*Z*)-**2**: δ(8-H) = 5.23 (calc.; ref. [8c], p. 118), 5.14 (det.); (7*E*)-**2**: δ(8-H) = 4.88 (calc.; ref. [8c], p. 118), 5.02 (det.); c) M. Hesse, H. Meier, B. Zeeh, *Spektroskopische Methoden in der organischen Chemie*, 4th ed, Thieme, Stuttgart, **1991**.
[9] Reaction of **1** with LiCl (excess) in acetic acid for 3 h at room temperature gave a mixture of (7*E*)-**2** and (7*Z*)-**2** with a yield of 35%.
[10] Compare P. J. Stang, V. V. Zhdankin in *Supplement C2: The Chemistry of Triple-bonded Functional Groups* (Ed.: S. Patai), Wiley, New York, **1994**, p. 1146–1147; reaction of **2** with lithium diisopropylamide in THF for 30 min at 0 °C gave **1** with 20% yield.
[11] **3** (only data differing from **1**): IR (KBr): $\tilde{\nu}$ = 1749, 1711, 1676, 1150 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.41 (overlapping, 1 H, 4-H), 7.12 (d, J = 12.4 Hz, 1 H, 5-H), 2.39 (overlapping, 2 H, 8-H), 1.70 (quint., J = 7.2 Hz, 2 H, 9-H), 2.08 (q, J = 7.2 Hz, 2 H, 10-H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 112.8 (C-4), 136.5 (C-5), 170.9 (C-7), 33.4 (C-8), 24.5 (C-9), 26.4 (C-10); DCI-MS (NH_3): m/z = 317.1715 (calc. for $[M-H]^-$: 317.1753).
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[16] Tuberculosis Antimicrobial Acquisition & Coordinating Facility of the National Institute of Allergy and Infectious Diseases, Birmingham, AL, USA; in this test, rifampicin had a IC_{98} value of 0.25 μg mL^{-1}.

π-Stacked *ortho*-Palladated Bipyridine Complexes Exhibiting Unusual Liquid Crystalline Behavior[**]

Abdelkrim El-ghayoury, Laurent Douce,
Antoine Skoulios, and Raymond Ziessel*

Liquid crystals (LCs) have many important applications, for example in the manufacture of visual display units or temperature sensors. Despite extensive and elegant investigations of their morphological properties, it is still hazardous to predict their precise structural behavior. Several major classes of LCs have been identified, such as nematic, smectic, and columnar, and crude guidelines have been established to specify the molecular requisites for LC properties. The design of an efficacious LC requires careful consideration of the molecular architecture that might induce the formation of the desired LC and, in some cases, also the prediction of molecular interactions in the emerging mesophase. In fact, mesomorphic materials provide some of the best examples of intermolecular interaction or self-assembly at the supramolecular level.

In the search for new LCs, metal-containing mesogens (metallomesogens) have recently attracted considerable attention owing to the possibility of combining the properties of the metal (color, magnetism, polarizability, redox behavior, electronic charge, resistivity, etc.) with those of the organic framework.[1, 2] Such substances have tremendous potential as

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